AMENDED CLAIMS

[received by the International Bureau on 27 April 2004 (27.04.04);
original claims 1-30 replaced by new claims 1-29 (4 pages)]

1. A formulation of a therapeutic substance suitable for delivery to a patient by a metered dose inhalation device, the formulation comprising a substantially dry powder preparation of the substance in association with a stabilising amount of a glycoside and a polyhydroxylated polyalkene in combination with one or more propellants therefor, wherein the therapeutic substance is selected from peptides and proteins.

2. A formulation according to claim 1, further comprising a cosolvent for said substance.

3. A formulation according to any preceeding claim, wherein the therapeutic substance is selected from antibodies, interferons, enzymes, hormones, euprolide acetate, CFTR, and α1-antitrypsin.

4. A formulation according to claim 3, wherein the therapeutic substance is a hormone selected from insulin, LHRH, granulocyte-colony stimulating factor, calcitonin, heparin, human growth hormone, and parathyroid hormone.

5. A formulation according to claim 1, wherein the substance is dnase I.

6. A formulation according to any preceding claim, which is non-immunogenic.

7. A formulation according to any preceding claim which is capable of being stored at room temperature without losing more than 50% biological activity of the therapeutic substance after two months.

8. A formulation according to any preceding claim, wherein the glycoside comprises at least one oligosaccharide.

9. A formulation according to claim 8, wherein the glycoside comprises at least one disaccharide.

10. A formulation according to claim 9, wherein the disaccharide is selected from trehalose, mannitol, sucrose, and mixtures thereof.

11. A formulation according to any preceding claim, wherein the glycoside constitutes between about 30% and 400% by weight of the therapeutic substance.

12. A formulation according to any preceding claim, wherein the propellant is alkane based.

13. A formulation according to claim 12, wherein the propellant is at least one haloalkane.

14. A formulation according to claim 13, wherein the propellant is selected from HFA-134a and HFA-227.

15. A formulation according to any preceding claim, wherein at least one polyhydroxylated polyalkene has the general structure

$$-(CH_2\text{-}CHOR)_n-$$

where R is the same or different from one monomeric unit to the next, and is hydrogen, lower alkyl, lower alkenyl, lower alkanoyl, lower alenoyl or is a bridging group between adjacent monomers.

16. A formulation according to claim 15, wherein, when R is not hydrogen, the number of carbon atoms, excluding any –CO- group, is between 1 and 6, inclusive.

17. A formulation according to claim 15 or 16, wherein the polyhydroxylated polyalkene is selected from polyvinylalcohol, polyvinylacetate, polyvinyl alcohol-*co*-vinyl acetate, poly(vinyl butyral), poly(vinyl alcohol-*co*-ethylene), and mixtures thereof.

18. A formulation according to claim 17, wherein the polyhydroxylated polyalkene is PVA.

19. A formulation according to claim 17 or 18, wherein the PVA a hydrolysate of PVAc, the level of hydrolysis being between 40% and 100%.

20. A formulation according to claim 17 or 18, wherein the PVA a hydrolysate of PVAc, the level of hydrolysis being between 50 and 90%.

21. A formulation according to any of claims 17 to 20, wherein the PVA has a molecular weight of between about 9 kDa and 50 kDa.

22. A formulation according to any preceding claim, wherein the polyhydroxylated polyalkenes are present in an amount of from about 5% to about 200% by weight of the therapeutic substance.

23. A formulation according to claim 22, wherein the polyhydroxylated polyalkene is present between about 10% and about 50% by weight of the substance.

24. A method for the preparation of a formulation as defined in any preceding claim, comprising blending the therapeutic agent with the glycoside and polyhydroxylated polyalkene substances in an aqueous vehicle, drying the resulting blend to a powder, and then formulating with propellant.

25. A method according to claim 24, wherein the aqueous vehicle is selected from saline, a suitable buffer, and deionised water.

26. A method according to claim 24 or 25, which comprises spray—drying the blend.

27. A powdered formulation of a therapeutic agent, a glycoside and a polyhydroxylated polyalkene, as defined in any of claims 1 to 23, which is suitable for incorporation with a haloalkane propellant for dispensing from a metered dose inhaler.

28. A powdered formulation according to claim 27, wherein the powder particles have an aerodynamic diameter of between about 1μm and 50μm.

29. A metered dose inhalation device provided with a reservoir comprising a formulation according to any of claims 1 to 23.